UNITED STA DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/308,150	09/30/99	VAN VENROOIJ W	30394-1027

005179
PEACOCK MYERS AND ADAMS P C
P O BOX 26927
ALBUQUERQUE NM 87125-6927

HM12/0130

EXAMINER	
DECLOUX, A	
ART UNIT	**PAPER NUMBER**
1644	13

DATE MAILED: 01/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/308,150	Van Venrooroolj et al.
Examiner	**Group Art Unit**
DeCloux, Amy	1644

☒ Responsive to communication(s) filed on *facsimiiled on 11/10/2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-15* is/are pending in the applicat

Of the above, claim(s) *10-14* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-9 and 15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

1. Applicant's election with traverse of Group II, Claims 1-3, and 5-7, drawn to a cyclic peptide, and the species of SEQ ID NO:10, in Paper No. 12, mailed 11-10-2000, is acknowledged. Applicants traverse the lack of unity on the ground(s) that the first claim does in fact provide a special technical feature that is distinguished over the prior art because applicants assert that the prior art dated 11-8-1997 is subsequent to the earliest filing date of the application which applicants assert is 11-15-1996, due to the filing of Netherlands application 1004539. However, examiner notes that the date needed in order to break unity of invention is the filing date of the 371 application which is 11-14-1997. Applicants also assert that certain of the applicants are among the authors of the referenced prior art. However the examiner notes that since the authorship of the referenced article is not identical to the inventive entity of the instant application, the art was done by another, absent a declaration to the contrary. However upon reconsideration the examiner has rejoined groups I, II and V, with the stipulation that Group V will be examined only to the extent of the part I of claim 15, IE "a method ...consisting of I) a peptide according to claim 1".

The requirement is still deemed proper and is therefore made final.

2. Claims 10-14 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with *37 C.F.R. § 1.48(b)* if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under *37 C.F.R. § 1.48(b)* and by the fee required under *37 C.F.R. § 1.17(h)*.

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

4. The following order or arrangement is preferred in framing the specification and, except for the title of the invention, each of the lettered items should be preceded by the headings indicated below.

(a) Title of the Invention.
(b) Cross-References to Related Applications (if any).
© Statement as to rights to inventions made under Federally-sponsored research and development (if any).
(d) Background of the invention.

1. Field of the Invention.
2. Description of the Related Art including information disclosed under *37 C.F.R. §§ 1.97-1.99.*

(e) Summary of the Invention.
(f) Brief Description of the Drawing.
(g) Description of the Preferred Embodiment(s).
(h) Claim(s).
(I) Abstract of the Disclosure.

5. Applicant should amend the first line of the specification to update the status (and relationship) of the priority documents. For example, "This application is a national stage filing under 35 USC 371 from PCT/xxxx/xxxxx, filed x/x/xxxx " should be inserted before the first sentence of the specification.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 5-9 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In the instant case, the specification does not convey to the artisan that the applicant had possession, at the time of invention, of the claimed peptides (with the exception of the peptides disclosed in Table 1) as recited in Claims 1-3, 5-9 and 15. Due to this broad definition of a peptide derived from any antigen recognized by any autoantibodies from patients with rheumatoid arthritis , none of these peptides (with the exception of the peptides disclosed in Table 1) meets the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See Vas-Cath, page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath, page 1116.).

The skilled artisan cannot envision all the contemplated peptides that are derived from any antigen recognized by any autoantibodies from patients with rheumatoid arthritis, even those with a formula according Formula I as recited in claim 2 and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only the peptides of Table 1 but not the full breadth of the instant claims, meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8. Claims 1-3, 5, 7-9 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide from Table 1 , consisting of SEQ ID NO:s 1-9, and a cyclic peptide consisting of SEQ ID NO:10, does not reasonably provide enablement for any peptide from any antigen recognized by autoantibodies from patients with rheumatoid arthritis as recited in the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention with any peptide other than those of SEQ ID NO:s 1-10 without an undue amount of experimentation. Other than the sequences of SEQ ID NO:1-10, the specification has not provided any biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies a) any peptides from any antigen wherein said peptide contains any modified arginine residue other than citrulline, or wherein said peptide is any peptidic fragment of profilaggrin, or wherein said peptide may be cyclized by any way other than through cysteine residues, and wherein said peptide reacts with autoantibodies from a

patient with rheumatoid arthritis as recited in the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make any of the recited peptides with the exception of SEQ ID NO:s 1-10, wherein said peptide would be reactive with autoimmune antibodies from a patient with rheumatoid arthritis, nor to use any of said peptides with the exception of SEQ ID NO:s 1-10 in a method for the detection of autoimmune antibodies as recited in claim 15, commensurate in scope with these claims. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

There is insufficient guidance in the instant specification to predict which sequence modifications of arginine in which peptides in which antigens will retain the ability to be reactive with autoimmune antibodies from a patient with rheumatoid arthritis. Predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which amino acids in the sequence, if any, are tolerant of modification and which are conserved or less tolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. differences effects the ability of said polypeptides to bind to an autoantibody, which would lead to undue experimentation, especially in view of the teachings of Abaza et al (J. Of Protein Chemistry, 11(5):433-444, 1992). Abaza et al show that even a single amino acid difference in an antigen may effect antibody binding by teaching that an amino acid substitution of myoglobin outside the epitope recognized by a monoclonal antibody causes the myoglobin to be unreactive with said antibody, (see entire article, especially the Abstract). Therefore predicting which peptides and modifications thereof, will retain the ability to bind autoantibodies in a patient with rheumatoid arthritis as recited in the instant claims , with the exception of SEQ ID NO:s 1-10, and therefore which peptides will be useful in a method of detection of autoimmune antibodies as recited in claim 15, is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

10. Claims 1-9 and 15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The phrase "corresponds to a part of a RNA molecule coding for the antigen, said part comprising a codon for an arginine residue," as recited in claim 1 and dependent claims 2-9 and 15, is not clear, because at the very least a codon of RNA would not encode a modification of arginine, and in particular does not apply to claim 7 for example which recites a synthetic peptide.

B) Claim 15 provides for the use of a peptide in a method for the detection of autoimmune antibodies, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

11. 35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title"

12. Claim 15 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

13. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention

thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, 2, 3, 7, 8 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Schellekens et al. (Arthritis and Rheumatism Vol. 40, No. 9 suppl. 8-12 November 1997)(in IDS)

Schellekens et al. teach synthetic peptides derived from an antigen that contains a modified arginine, specifically the modified arginine residue citrulline, and that they are reactive to antibodies specifically present in rheumatoid arthritis sera directed against filaggrin (see entire abstract). Schellekens et al. teach also that a method of detecting said antibodies could be detected in the in rheumatoid arthritis sera with an ELISA assay. Therefore, the referenced teachings anticipate the claimed invention.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

15. Claims 1, 2, 3, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Simon et al J. Clin. Invest. 92:11387-1393, 1993,(IDS), as evidenced by WO/ 99/35167.

Simon et al teach that filaggrin is recognized by auto-antibodies specifically in RA patients (see Abstract and page 1387, column 2, last sentence of second paragraph.). Therefore, the referenced teachings anticipate the claimed references. It is noted that even though the modification of Arginine was not taught, the claimed functional limitations would be inherent properties of the referenced peptides, as evidenced by WO/99/35167. '167 teaches that citrulline containing peptides of human filaggrin reacted with autoantibodies of rheumatoid arthritis (see entire article, especially the Abstract).

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone

number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D.
Patent Examiner,
Group 1640, Technology Center 1600
January 29, 2001

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644